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(to be used for all correspondence after initial filing)

Application Number	09/715,725
Filing Date	November 16, 2000
First Named Inventor	LUO, YING
Group Art Unit	1642
Examiner Name	UNGAR, SUSAN NMN
Total Number of Pages in This Submission: 23	Attorney Docket Number: RIGL-008CIP

ENCLOSURES (check all that apply)

- [ ] Fee Transmittal Form
  - [ ] Fee Attached
- [ ] Amendment / Reply
  - [ ] After Final
  - [ ] Affidavits/declaration(s)
- [ ] Extension of Time Request
- [ ] Express Abandonment Request
- [ ] Information Disclosure Statement
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- [ ] Response to Missing Parts/ Incomplete Application
  - [ ] Response to Missing Parts under 37 CFR 1.52 or 1.53
- [ ] Assignment Papers *(for an Application)*
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- [ ] Petition to Convert to a Provisional Application
- [ ] Power of Attorney, Revocation Change of Correspondence Address
- [ ] Terminal Disclaimer
- [ ] Request for Refund
- [ ] CD, Number of CD(s
- [ ] After Allowance Communication to Group
- [ ] Appeal Communication to Board of Appeals and Interferences
- [ ] Appeal Communication to Group *(Appeal Notice, Brief, Reply Brief)*
- [ ] Proprietary Information
- [ ] Status Letter
- [x] Other Enclosure(s) *(please identify below):*

Response to Notification of Non-Compliant Appeal Brief

Appeal Brief (Substitute)

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Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Signing Attorney/Agent (Reg. No.)	JAMES S. KEDDIE, PH.D., 48,920 BOZICEVIC, FIELD & FRANCIS, LLP
Signature	James S Keddie
Date	December 14, 2006

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Response to Notification of Non-Compliant Appeal Brief Address to: Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450	Attorney Docket No.	RIGL-008CIP
	Confirmation No.	6653
	First Named Inventor	LUO, YING
	Application Number	09/715,725
	Filing Date	November 16, 2000
	Group Art Unit	1642
	Examiner Name	UNGAR, SUSAN NMN
	Title: "*NOVEL IAPS ASSOCIATED CELL CYCLE PROTEINS, COMPOSITIONS AND METHODS OF USE*"	

Sir:

This communication is responsive to the Notification of Non-Compliant Appeal Brief dated December 4, 2006, for which a one month period for response was given making this response due on or before January 4, 2006.

A substitute Appeal Brief is submitted herewith.

The Notification of Non-Compliant Appeal Brief states that support for independent claims 26 and 29 must be pointed out in Appeal Brief, by referring to the specification by page and line number. In the substitute Appeal Brief, support for independent claims 26 and 29 is pointed by reference to the brief description of Figs. 7 and 8 in the specification. As agreed in a teleconference with Exr. Foley (SPE) on December 12, 2006, the Examiner's request and the requirements of 37 C.F.R. § 41.37(c)(1)(v) have been met.

The Examiner's comments on page 3 of the Notification of Non-Compliant Appeal Brief are noted.

The substitute Appeal Brief indicates the status of claim 28.

The Grounds of Rejection to be Reviewed on Appeal section of the Appeal Brief has been amended in accordance with the Examiner's suggestion.

The Applicants believe that the substitute Appeal Brief is in full compliance with 37 C.F.R. § 41.37.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number RIGL-008CIP.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: December 14, 2006

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APPEAL BRIEF
(SUBSTITUTE)

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Attorney Docket No.	RIGL-008CIP
Confirmation No.	6653
First Named Inventor	Ying Luo
Application Number	09/715,725
Filing Date	November 16, 2000
Group Art Unit	1642
Examiner Name	Susan Ungar
Title: NOVEL IAPS ASSOCIATED CELL CYCLE PROTEINS, COMPOSITIONS AND METHODS OF USE	

Sir:

This Brief is filed in support of Appellants' appeal or the rejections set forth in the Office Action dated May 5, 2006, 2006. A Notice of Appeal was filed on February 10, 2006.

The Commissioner is hereby authorized to charge deposit account number 50-0815 to cover any fee required for filing this brief.

TABLE OF CONTENTS

REAL PARTY IN INTEREST

The real party in interest in this case is Rigel Pharmaceuticals, Inc.

RELATED APPEALS AND INTERFERENCES

There are no appeals pending which would directly affect, be directly affected by, or have a bearing on the Board's decision in the instant appeal.

STATUS OF CLAIMS

Claims 26, 27, 29, 30 and 32 are pending. Rejections of claims 26, 27, 29, 30 and 32 are appealed herein.

Claims 1-25, 28 and 31 are cancelled.

STATUS OF AMENDMENTS

No amendments to the claims were filed subsequent to issuance of the prior Office Action.

SUMMARY OF CLAIMED SUBJECT MATTER

The pending claims are directed to a recombinant ING2 protein. Wild-type ING2 protein has a high level of sequence identity to ING1 (Fig. 11 and page 6, line 20), a protein that has been well characterized structurally and functionally (page 7, lines 12-24). The instant specification shows experimental results demonstrating that ING2, like ING1, cooperates with the well known tumor suppressor p53 in activating transcription of p53-inducible promoters (Fig. 12; page 7, lines 8-10). The claims encompass ING2 proteins that are encoded by a nucleotide sequence of SEQ ID NO:7 (see, e.g., page 5, lines 15-16 and Fig. 7) as well as ING2 proteins having at least 95% sequence identity to the amino acid sequence of SEQ ID NO:8 (see, e.g., the polypeptide encoded by SEQ ID NO:7; page 5, lines 17-18 and Fig. 8).

Claim 26 recites a recombinant ING2 protein encoded by the contiguous polynucleotide sequence of nucleotides 120-845 of the nucleic acid set forth in SEQ ID NO:7 (page 5, lines 15-16 and Fig. 7).

Claim 27 recites a recombinant ING2 protein comprising an amino acid sequence having at least 95% sequence identity to the contiguous sequence set forth in SEQ ID NO:8 (page 7, lines 31-35), where the recombinant ING2 protein increases activity of a promoter having a p53 binding site when introduced into a mammalian cell (page 7, lines 8-10 and page 33, lines 5-6).

Claim 29 recites a recombinant ING2 protein consisting essentially of the contiguous amino acid sequence set forth SEQ ID NO:8 (page 5, lines 17-18 and Fig. 8).

Claim 30 is dependent on claim 29 and recites a recombinant ING2 protein that increases activity of a promoter having a p53 binding site when introduced into a mammalian cell (page 7, lines 8-10 and page 33, lines 5-6).

Claim 32 is dependent on claim 27 and recites a recombinant ING2 protein that has the contiguous amino acid sequence set forth in SEQ ID NO:8 (page 5, lines 17-18 and Fig. 8).

GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

1. Whether claims 26-27, 29-30 and 32 are unpatentable under 35 U.S.C. § 112, first paragraph, as being based on a non-enabling disclosure

2. Whether claims 27, 30 and 32 are unpatentable for not meeting the written description requirement of 35 U.S.C. § 112, first paragraph

3. Whether claim 27 is unpatentable for not meeting written description requirement of 35 U.S.C. § 112, first paragraph

4. Whether claim 27 is unpatentable under 35 U.S.C. § 112, first paragraph, as being based on a non-enabling disclosure

ARGUMENTS

1. Rejection of claims 26-27, 29-30 and 32 under 35 U.S.C. § 112, first paragraph (enablement)

Claims 26-27, 29-30 and 32 are rejected as failing to meet the enablement requirement of 35 U.S.C. § 112, first paragraph. Summarizing an eight page rejection, the Examiner argues that the claimed ING2 polypeptides have questionable utility and, as such, the specification does not enable one of skill in the art to use the claimed subject matter. This enablement rejection is grounded on a "lack of utility" basis.

MPEP § 2164.07I.A very clearly states, however, that if there is no basis for rejecting claims under 35 U.S.C. § 101, there is also no basis for an enablement rejection grounded on a "lack of utility" basis.[1] In other words, according to MPEP § 2164.07I.A, this rejection should not be imposed unless it is also accompanied by a rejection under 35 U.S.C. § 101.

Claims 26-27, 29-30 and 32 are *not* rejected under 35 U.S.C. § 101. There is no

[1] MPEP § 2164.07I.A: "Office personnel should not impose a 35 U.S.C. 112, first paragraph, rejection grounded on a "lack of utility" basis unless a 35 U.S.C. 101 rejection is proper."

question about the utility of the subject matter of the claims.

Since there is no accompanying rejection under 35 U.S.C. § 101, in accordance with MPEP § 2164.07I.A, this rejection lacks merit and should be reversed.

In attempting to establish this rejection, the Examiner asserts there is no nexus between SEQ ID NO:8 and either ING2b or ING2c (data is provided for ING2b (SEQ ID NO:4) and ING2c (SEQ ID NO:6) showing activation of p53, a well known tumor suppressor), and thus SEQ ID NO:8 has no use.[2] *The grounds for this enablement rejection are substantially identical to the grounds to support the prior utility rejection under §101,*[3] *which was withdrawn in view of Applicants' arguments earlier in prosecution.*

The Examiner's maintenance of a rejection under 35 U.S.C. §112, first paragraph, on the same grounds that were the basis of a rejection under 35 U.S.C. § 101 both inconsistent with the law, and the Patent Office requirement for Examiners to efficiently examine applications and avoid "piecemail" prosecution.[4]

As detailed in prior responses, SEQ ID NOS: 2, 4, 6, 8 and 10, as well as p28ING5 (see, Shiseki *et al.* Cancer Research 63: 2373-2378, 2003) are splice variants encoded by the same gene, and all share a 200 amino acid domain. As shown in Fig. 12 of the instant specification and in Shiseki *et al*, each of ING2b, ING2c and p28ING5 regulate expression from p53 binding site promoters. In view of this data and the high relatedness of the members of the ING2 family, one of skill in the art would reasonably conclude that SEQ ID NO:8 has uses that are enabled by the instant specification, e.g., in screening assays for identifying agents that modulate p53 activity and the cell cycle (see, e.g., page 35, line 32 to page 36, line 19).

The utility of SEQ ID NO:8 is not in any doubt. Since this rejection is based on the Examiner's notion that the claimed subject matter has questionable utility, this rejection should be reversed.

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[2] Office Action mailed August 10, 2005, page 3, lines 10-11 and page 4, lines 21-23.

[3] See Office Action mailed August 8, 2003, pages 4-12.

[4] MPEP § 707.07(g): Piecemeal examination should be avoided as much as possible.

Reversal of this rejection under 35 U.S.C. § 112, first paragraph (enablement based on lack of utility) is respectfully requested.

2. Rejection of claims 27, 30 and 32 under 35 U.S.C. § 112, ¶1 (written description)

Claims 27, 30 and 32 are rejected as failing to meet the written description requirement of 35 U.S.C. § 112, first paragraph. The basis for this rejection is the Examiner's belief that the claims 27, 30 and 32 recite subject matter that is broader than as described in the specification as originally filed.[5]

The written description requirement of 35 U.S.C. § 112, first paragraph, involves the question of whether the subject matter of a claim conforms to the disclosure of an application as filed. According to the MPEP, an objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed?"[6] The subject matter of the claim need not be described literally (i.e. using the same terms or *in haec verba*) in order for the disclosure to satisfy the written description requirement[7].

According to page 11 of the Office Action, the Examiner appears to believe that the phrase "wherein said recombinant ING2 protein increases activity of a promoter having a p53 binding site", is not supported in the specification as filed.

The Appellants submit, however, that there is extensive and explicit support for ING2 proteins that increase the activity of a promoter having a p53 binding site at several places in the specification.

[5] See Office Action dated August 10, 2005, last paragraph.
[6] See MPEP § 2163.02, citing *In re Gosteli* 872 F.2d 1008, 1012 (Fed. Cir. 1989).
[7] See MPEP § 2163.02.

For example, support for such ING2 proteins can be found at:

- page 7, lines 8-9, stating that "ING2 activates p53 binding site controlled promoters in the presence of absence of p53";
- page 33, lines 5-6, stating that cell cycle proteins (of which ING2 is an example) "activate p53 binding site controlled promoters";
- page 37, line 3, stating that assay employing an ING2 polypeptide can include measuring "activation of p53 binding site controlled promoters"; and
- Fig. 12, which shows data demonstrating that ING2 proteins (of which SEQ ID NO:8 is an example) increases transcriptional activation by p53 in a mammalian cell.

In view of the above, the Appellants submit there is adequate support for the phrase "wherein said recombinant ING2 protein increases activity of a promoter having a p53 binding site".

The Appellants submit that the current claims recite subject matter that is no broader than as described in the specification as originally filed. As such, the Appellants believe that the written description requirement of 35 U.S.C. § 112, first paragraph, has been satisfied, and no new matter is added.

Reversal of this rejection is requested.

3. Rejection of claim 27 under 35 U.S.C. § 112, first paragraph (written description)

Claim 27 is rejected as not meeting the written description requirement of 35 U.S.C. § 112, first paragraph. In attempting to support this rejection, the Examiner argues that a genus of ING2 proteins that comprise an amino acid sequence having at least 95% identity to SEQ ID NO:8 and that increase activity of a promoter having a p53 binding sites are inadequately

described by the instant specification. The Examiner cites *Lilly*[8] and *Enzo*[9] in support of this rejection.

The Appellants submit that the fact pattern in the instant case falls squarely into the fact pattern of Example 14 of the Synopsis of Application of Written Description Guidelines[10] ("the Guidelines"; copy enclosed as Exhibit A).

The Appellants understand that he Patent Office has instructed Examiners to adhere to the law as summarized in the Guidelines. While certainly the Guidelines would be subservient to the law, the Examiner has cited no Board, Federal Circuit or Supreme Court decision that renders the Guidelines inapplicable. Indeed, the Federal Circuit itself has pointed to these very Guidelines in recent decisions in assisting the analysis of written description issues.[11] As such, the Guidelines should be followed, not ignored.

The Appellants submit that if the Guidelines are followed, claim 27 meets the written description requirement of §112, first paragraph.

Example 14 of the Guidelines describes a scenario very similar to that currently under examination.

In Example 14, the claim is directed to "A protein having SEQ ID NO:3 and variants thereof that are at least 95% identical to SEQ ID NO: 3 and catalyze the reaction of A->B." The language of the claim of Example 14 is almost identical to rejected claim 27. The Example 14 claim and claim 27 recite a specific sequence and a functional activity. The claim of Example 14 and claim 27 are therefore of similar in type and kind.

The specification of Example 14 discloses a polypeptide sequence of SEQ ID NO:3 as having a certain activity.[12] The specification of Example 14 also "contemplates but does not exemplify" variants of SEQ ID NO:3, and provides an assay for measuring the activity of the protein.

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[8] *University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997)

[9] *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 269 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002)

[10] "Synopsis of Application of Written Description Guidelines", as published to the world wide website of the U.S.P.T.O. on March 1st, 2000.

[11] See Enzo Biochem v Gen-Probe 296 F3d 1316 (Fed. Cir. 2002)

Again, the fact pattern of Example 14 is very similar to the instant fact pattern. The instant specification: a) describes the sequence of a full length polypeptide (i.e., SEQ ID NO:8), b) describes that SEQ ID NO:8 has IAP (for ""*I*nhibitor of *A*poptosis *P*rotein") binding activity (see page 33, lines 4-5) and p53-modulatory activity (see, e.g., Fig. 12; page 7, lines 8-10); and c) provides detailed methods of how IAP binding activity and p53 modulatory activity can be assayed (see e.g., page 42, lines 16-27 and Fig. 12 of the instant specification). In addition, a total of *five* similar ING2 isoforms, ING2A, ING2B, ING2C, ING2D and ING2E (corresponding to SEQ ID NOS: 2, 4, 6, 8 and 10, respectively) are described in the instant specification. The amino acid sequences of these proteins are shown in the sequence alignment of Fig. 11. As such, the Applicant's claims are supported by *five* examples, of ING2 proteins, not one.

The Guidelines state that the claim of Example 14 is adequately described by the specification and the requirements of 35 USC §112 first paragraph have been met because:

> "The single species disclosed is representative of the genus because all members have at least 95% structural identity with the reference compound and because of the presence of an assay which applicant provided for identifying all of the at least 95% identical variants of SEQ ID NO: 3 which are capable of the specified catalytic activity."

The claim of Example 14 and rejected claim 27 contain limitations that are similar in type and kind. The specification of Example 14 and the instant specification both describe a representative sequence, as well as a functional activity and an assay by which the activity can be measured.

In view of the similarity between the fact pattern of the Example 14 and the fact pattern described in Example 14 of the Guidelines, the Appellants submit that claim 27, like the claim of Example 14, meets the written description requirement of §112,¶1.

The Patent Office Guidelines are provided to Examiners for good reason: to promote consistent application of the law to claims of similar subject matter. This not only serves the Patent Office's goal of efficient prosecution, but also provides applicants with guidance as to

[12] SEQ ID NO:3 encodes a polypeptide having ligase activity

how they can reasonably expect the law to be applied. Here, the Examiner has elected to wholly ignore the Patent Office's own guidelines, resulting in protracted prosecution of the instant claims and increased cost to the Applicants.

In rendering its decision, the Board is respectfully requested to clear that, to the extent the Guidelines are and remain good law, Examiners should apply them.

The Applicants finally note that reversal of this rejection would be consistent with recent decisions by the Board of Patent Appeals and Interferences of the United States Patent and Trademark Office. The decisions are and *Ex parte Bandman* BAPI Appeal No. 2004-2319 (2004) and *Ex parte Sun* BAPI Appeal No. 2003-1993 (2003), among others. The genus claims that are the subject of in these decisions were supported by disclosure of a *single* representative species encompassed by the claims. Since the instant claims are supported by *five* examples, the Applicants submit that the instant claims should well satisfy criteria used by the Board for withdrawing this type of rejection.

Reversal of this rejection is respectfully requested.

4. Rejection of claim 27 under 35 U.S.C. § 112, fist paragraph (enablement)

Claim 27 is rejected as not meeting the enablement requirement of 35 U.S.C. §112, first paragraph. In attempting to support this rejection, the Examiner argues that a genus of ING2 proteins that comprise an amino acid sequence having at least 95% identity to SEQ ID NO:8 and that increase activity of a promoter having a p53 binding sites are not enabled by the instant specification.

In order to satisfy the enablement requirement of 35 U.S.C. § 112, first paragraph, the Office is reminded that extensive experimentation may be performed, as long as the experimentation is routine, and that every species within a genus does not have to be operative for a claim to be fully enabled.[13]

[13] *In re Certain Limited-Charge Cell Culture Microcarriers*, 221 USPQ 1165, 1174 (Int'l Trade Comm'n 1983), *aff'd sub nom., Massachusetts Institute of Technology v. A.B. Fortia*, 227 USPQ 428 (Fed. Cir. 1985). *Hybritech v. Monoclonal Antibodies, Inc.* 231 USPQ 81 (Fed. Cir. 1986)

This rejection is based on the idea that biological systems are complex and unpredictable and, as such, one of skill in the art would not know which amino acids of the claimed ING2 protein could be changed without changing the function of the protein.

The Appellants are aware that biological systems can, in certain circumstances, be complex and unpredictable. The Appellants submit, however, that the instant specification, combined with what is already known about related the related ING1, which is a highly characterized protein and has a function similar to ING2, provides sufficient guidance as to which amino acids could be changed in ING2 in order for it to remain functional. As such, the Appellants believe that no undue experimentation would be required to practice what is being claimed.

Factual support for the Appellants position is set forth below:

With regard to ING2 protein domains that are important for ING2 function, a skilled person would look towards Fig. 11 of the specification, and what is known in the art about the structure and function of the highly related ING1 protein, which is shown aligned with the subject ING2 isoforms in Fig. 11, for guidance. Fig. 11 of the instant application is reproduced below.

Fig. 11 shows an alignment of the subject ING2 isoforms with other ING proteins, including ING1. ING1, as described on page 7 of the instant specification, is highly characterized and has a role in apoptosis that appears to be similar to that of ING2. Residues that are conserved between two or more proteins shown in this alignment as highlighted in black boxes. This alignment therefore shows several regions that are conserved between the various ING proteins, including, in particular, several conserved amino acids at the C-terminus of the protein, and a large region of amino acids at the C-terminus of the protein, starting from the "DPNEPTY..." and finishing at ".....TTKPKGKW".

Since ING1 and ING2 are functionally similar and contain several regions of conserved amino acids, including a large block of conserved amino acids at their C-termini, a skilled person would instantly recognize that these domains may be important for function of ING proteins. Moreover, the fact that these domains are conserved among the different ING2 isoforms themselves further suggests to the skilled person that these domains are less preferred for introduction of amino acid changes, particularly those non-conservative amino

acid changes. A skilled person would generally avoid making amino acid changes in these regions when designing ING2 variants that are at least 95% to SEQ ID NO:8.

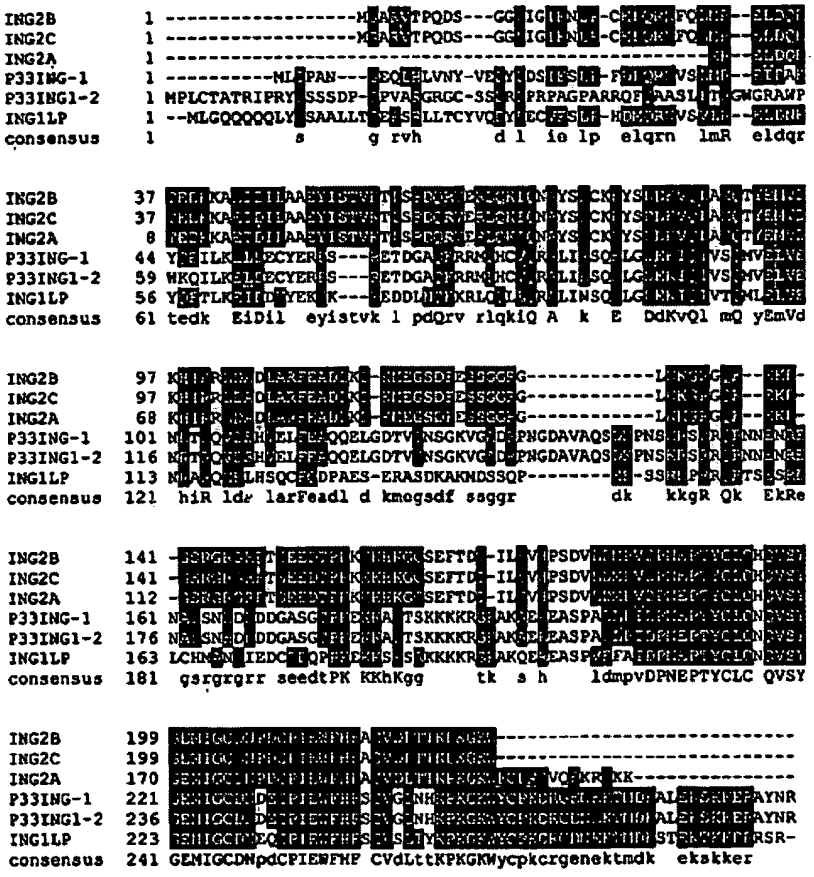
With the knowledge that ING1 and ING2 have apoptosis activity and have conserved domains, a skilled person would, for example, swap domains from ING1 to ING2 (i.e. SEQ ID NO:8) with an expectation that the resultant protein would retain an apoptosis activity.

Further, a skilled person, upon viewing the instant specification, particularly Figure 11 would have knowledge of the prior art regarding the structure/function relationship of ING proteins, and would apply this knowledge in the production of claimed ING2 variants. For example, one of skill in the art would have knowledge of all of the papers referenced on page 7, lines 22-24, of the instant specification, i.e., Helbing *et al.*, *A novel candidate tumor suppressor, ING1, is involved in the regulation of apoptosis*. Cancer Res. 1997 57:1255-8; Garkavtsev et al., *Suppression of the novel growth inhibitor p33ING1 promotes neoplastic transformation*. Nat Genet. 1996 14:415-20; Garkavtsev et al., *The candidate tumour suppressor p33ING1 cooperates with p53 in cell growth control*. Nature. 1998 Jan 15;391(6664):295-8; and Shimada et al., *Cloning of a novel gene (ING1L) homologous to ING1, a candidate tumor suppressor* Cytogenet Cell Genet. 1998 83:232-5.

In particular, Zeremski (J. Bio. Chem. 1999 *Structure and regulation of the mouse ing1 gene. Three alternative transcripts encode two phd finger proteins that have opposite effects on p53 function* 274:32172-32181; copy enclosed as Exhibit B), discusses several amino acids that are conserved between ING proteins (see Fig. 4B on page 32177 and abstract), and indicates that the conserved C-terminal domain is a "PHD" DNA binding domain (see page 32180, second column). Most of the conserved amino acids of Zeremski's sequence alignment are also indicated as being conserved in the alignment of Fig. 11. While not relied upon to make this assertion, Zeremski confirms the conserved amino acids identified in Fig. 11, and assigns an art-recognized domain name and function to the conserved C-terminal region.

A skilled person would also look towards the sequence alignment shown in Fig. 11, as well what is known in the art about the structure of the ING1 protein for guidance in making variants of ING2.

Fig. 11 is reproduced below.



As shown in Fig. 11, ING2 proteins are highly related to ING1, a highly characterized protein having a function similar to SEQ ID NO:8.[14] When provided the sequence alignment Figure 11, the skilled person, who also has extensive knowledge of several publications on the structure/function relationship of ING1 proteins, would note the conserved and non-conserved regions and amino acids between the various ING proteins in the alignment and readily use this knowledge to produce functional variants of SEQ ID NO:8. For example, the skilled person would recognize a large number of amino acids in an ING2 protein having the sequence of SEQ ID NO:8 that may be substituted, and reasonably expect that these substitutions would have no significant effect on its function.

[14] ING1 in the prior art, but is not within the scope of claim 27.

The bottom line of the ING sequences shown in Figure 11 shows a "consensus" sequence. This consensus sequence shows amino acids that are conserved in all ING proteins shown (indicated in upper case letters). Residues conserved in more than two ING proteins (but not all ING proteins) are shown in lower case letters. Since all the ING proteins shown in the figure have a conserved function, a skilled person would recognize that, in order to make ING2 variants, amino acids at positions that correspond to upper case letters in the consensus sequence should would be less preferred sites for modification, and that amino acids that correspond to lower case letters in the consensus sequence may be modified to any other amino acid at that position.

Further, at positions in which there is no amino acid listed in the consensus sequence, a skilled person may be able to choose any amino acid at that position. A skilled person would also recognize that certain amino acids may be substituted by another amino acid having a similar property. For example, D (Asp) and E (Glu) are acidic resides and may be substituted by each other. Likewise, it is well knows that K (Lys) and R (Arg) are basic residues and may be substituted by each other, S (Ser) and T (Thr) are polar, uncharged, hydroxyl-containing residues and may be substituted by each other, and that L (Leu), I (Ile) and V (Val) non-polar residues that may be substituted by each other.

In other words, by simply looking at the sequence alignment shown in Fig. 11, a skilled person would instantly recognize a large number of amino acids in an ING2 protein having the sequence of SEQ ID NO:8 that may be substituted, and reasonably expect that these substitutions would have no significant effect on ING2 function.

Finally, the Appellants note that the specification provides working examples of *five* ING2 isoforms, ING2A, ING2B, ING2C, ING2D and ING2E (corresponding to SEQ ID NOS: 2, 4, 6, 8 and 10, respectively) are described in the instant application. ING2A, ING2B, ING2C and ING2E share 87.6%, 94.2%, 94.2% and 81.8% amino acid sequence identify to ING2D (corresponding to SEQ ID NO:8), respectively. Considering each of ING2A, ING2B, ING2C, ING2D and ING2E bind IAP and can induce p53 expression (see Fig. 12 of the instant specification), a skilled person would reasonably expect ING2 variants with *at least 95% identity* (i.e., significantly greater than 81.8% identity) to SEQ ID NO:8 to have an activity similar to that of SEQ ID NO:8.

In summary, the specification provides adequate evidence that one can substantially modify the amino acid sequence of an ING2 protein, without loss of function. Since ING1 (which has as little as 81.8% identity to an ING2 protein) has a function similar to that of ING2, a skilled person would recognize that ING proteins with at least 95% sequence identity to an ING2 protein could be made and used without undue experimentation.

In view of the foregoing discussion, the Appellants submit that the instant specification provides sufficient guidance as to which amino acids could be changed in an ING2 variant having the sequence of SEQ ID NO:8 in order for it to remain functional. As such, the Applicants believe that no undue experimentation is required to practice the subject matter of claim 17, and this rejection should be reversed.

Reversal of this respectfully requested.

SUMMARY

The Appellants submit that all current rejections lack merit.

RELIEF REQUESTED

The Appellants respectfully request that all of the rejections be reversed, and that the application be remanded to the Examiner with instructions to issue a Notice of Allowance.

Respectfully submitted,

Date: December 14, 2006

By: _____
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Claims Appendix

1-25. (Cancelled)

26. A recombinant ING2 protein encoded by the contiguous polynucleotide sequence of nucleotides 120-845 of the nucleic acid set forth in SEQ ID NO:7.

27. A recombinant ING2 protein, comprising an amino acid sequence having at least 95% sequence identity to the contiguous sequence set forth in SEQ ID NO:8, wherein said recombinant ING2 protein increases activity of a promoter having a p53 binding site when introduced into a mammalian cell.

28. (Cancelled)

29. A recombinant ING2 protein, consisting essentially of the contiguous amino acid sequence set forth SEQ ID NO:8.

30. The recombinant ING2 protein of claim 29, wherein said ING2 protein increases activity of a promoter having a p53 binding site when introduced into a mammalian cell.

31. (Cancelled)

32. The isolated protein of claim 27, wherein said isolated protein has the contiguous amino acid sequence set forth in SEQ ID NO:8.

EVIDENCE APPENDIX

No evidence submitted under 37 CFR §§ 1.130 or 1.131 has been relied upon by Appellants in this Appeal.

Exhibits A and B are appended hereto.

Exhibit A: Example 14 of the "Synopsis of Application of Written Description Guidelines", as published to the world wide website of the U.S.P.T.O. on March 1st, 2000.

Exhibit B: Zeremski et al. (J. Biol. Chem 274:32172-32181, 1999). This reference is of record.

RELATED PROCEEDINGS APPENDIX

There are no decisions rendered by a court or the Board which would directly affect or be directly affected by, or have a bearing on the Board's decision in the instant appeal.